UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

SCHERING CORPORATION, et al., Plaintiffs, v. MYLAN PHARMACEUTICALS, INC., et al., Defendants.	Civil Action No.: 09-6383 (JLL) **OPINION**

LINARES, District Judge.

This matter comes before the Court on Plaintiff's allegations of patent infringement by Defendant. Defendant concedes infringement but argues that Plaintiff's patent is invalid and unenforceable. After a bench trial the Court finds, for the foregoing reasons, that Plaintiff's patent is valid and enforceable. The Court further finds that Defendant's allegations of inequitable conduct are without merit.

I. BACKGROUND

Plaintiff Schering Corporation ("Schering") is a New Jersey corporation with its principal place of business at 2000 Galloping Hill Road, Kenilworth, NJ. Plaintiff MSD International GmbH is a Swiss Corporation having a registered address at Weystrasse 20, 6000 Lucerne 6, Switzerland. Defendant Mylan Pharmaceuticals, Inc. ("Mylan") is a West Virginia corporation with a principal place of business at 781 Chestnut Ridge Road, Morgantown, West Virginia. Mylan's parent company, Mylan, Inc., has entered into a stipulation to be bound by the results of this case.

This is an action for patent infringement arising as a result of Mylan's filing two Abbreviated New Drug Applications ("ANDA") Nos. 200-082 and 201-790 with the U.S. Food and Drug Administration ("FDA") seeking approval to manufacture and sell generic versions of Vytorin® and Zetia® prior to the expiration of U.S. Patent No. RE42,461 (the "'461 Patent") (PX 8) and U.S. Patent No. 5,5846,966 (the "'966 Patent"). Plaintiffs have withdrawn many of their original claims including claim 3 of the '461 patent and all asserted claims of the '966 patent, so that the only remaining claims in this litigation are claims 10-13 of the '461 patent. For the purpose of this litigation, Mylan admits that Mylan's generic products, if approved, would infringe these disputed claims. Accordingly, the issue before the Court is whether Mylan has proved that the '461 patent is invalid and unenforceable.[1]

A. The '461 Patent-in-Suit

The '461 patent is a reissue of U.S. Patent RE37,721 (the "'721 Patent") (DTX 512). The '721 Patent, in turn, is a reissue of U.S. Patent 5,767,115 (the "'115 patent") (DTX 507). U.S. Patent 5,631,365 (the "'365 Patent") contains essentially the same specification as the '461, '721, and the '115 but is limited to process claims for making beta-lactam compounds. The sole inventor on the '365 Patent is Stuart Rosenblum ("Rosenblum"). The named inventors on the '461, '721, and '115 patents are Drs. Stuart Rosenblum, Sundeep Dugar ("Dr. Dugar"), Duane Burnett ("Dr. Burnett"), John Clader ("Dr. Clader"), and Brian McKittrick ("Dr. McKittrick").

The first patent application in this group was U.S. Application Serial No. 08/102,440

[1]The Court has deferred consideration of whether this case is an exceptional case, warranting the award of attorneys' fees under 35 U.S.C. § 2385, until after the Court has decided the validity and enforceability issues.

(the "'440 Application") filed September 21, 1993. (PX 452). The initial '440 application lists Drs. Rosenblum, Dugar, Burnett, and Clader as inventors. This application broadly claims a genus of approximately a quintillion beta-lactams that include hydroxy-substituted azetidones. (PX 452). The '440 application does not disclose compounds 4E, 4F, 6C, 6D and ezetimibe.

Schering subsequently abandoned the '440 application and, in its place, filed two continuation-in-part applications, U.S. Application Serial No. 08//257,593 on June 9, 1994, and International Patent Application PCT/US94/10094, on September 14, 1994. These applications matured into the '115 and the '721 patents. Thus, the effective filing date of the '461 patent is no later than June 9, 1994.

Compounds 4E, 4F, 6C, 6D and ezetimibe were first disclosed in the '115 patent. (DTX 507). The '115 patent also disclosed the methods for purportedly synthesizing these compounds. (DTX 510). The '115 patent later reissued as the '721 patent, which also claims those same compounds but added specific bullet claims to ezetimibe. (See DTX 512 at claims 10-13). The '721 patent later reissued as the '461 patent. (PX 8 at 1.) Compounds 4E, 4F, 6C, 6D were removed from the claims of the '461 patent during the reissue process, however the bullet claims to ezetimibe remain.

Notably, International Patent Application PCT/US92/05972 names Drs. Burnett and Clader as co-inventors. This application published as International Patent Publication No. WO 93/02048 (the "'048 PCT") on February 4, 1993, more than a year before the earliest effective filing date of the '461 patent. (DTX 1219.) The title of the '048 PCT is "Substituted Beta Lactam Compounds Useful as Hypocholesterolemic Agents and Processes for the

Preparation Thereof." (DTX 1219). However, unlike the filings in the '461 patent, the '048 PCT discloses non-hydroxylated azetidinone compounds. Schering contends that the '440 application and the '048 PCT discloses operative methods for making compounds 4E, 4F, 6C, and 6D and therefore, the named inventors were, as of said time, cognizant of an operative method for making these compounds before Dr. Afonso synthesized these compounds in December 1993. In the instant litigation, Dr. Rosenblum testified that five of the seven methods disclosed in the '440 application would work to synthesize compounds 4E, 4F, 6C, and 6D. Schering's expert, Roush, contends that only three methods: A, D and F, could be used to synthesize these compounds. Mylan maintains that none of the methods disclosed in the '440 application or the '048 PCT would have been operative methods for making Compounds 4E, 4F, 6C and 6D.

B. The Schering ACAT/CAI

The evidence presented at trial set forth that on or about 1988, Schering began a research program to develop an Acyl-coenzyme A cholesterol acyltransferase enzyme ("ACAT"), which was believed to be involved in the absorption of cholesterol from food, and accordingly, treat heart disease. Some years later, Schering changed the name of the program to the Cholesterol Absorbtion Inhibition ("CAI") project. Dr. Clader was the CAI project leader in the early and mid-1990s and was the section leader of the atherosclerosis group. During that time, Dr. Ashit Ganguly ("Dr. Ganguly") was Vice President of Chemistry and Green was Director of Chemical Research at Schering. The CAI project involved contributors from the biology, chemistry, and metabolism groups within Schering.

The chemists working on the project synthesized prospective drug compounds. When

a new compound was synthesized, its expected structure could generally be predicted based on the starting materials used and reaction scheme that followed. Chemical structure was confirmed using proton nuclear magnetic resonance ("proton NMR's"), C13 nuclear magnetic resonance, high performance liquid chromatography, mass spectometry, and/or infrared spectrometry. The new compounds were typically then tested in two biological evaluations: *in vitro* lab tests and *in vivo* live hamster tests. Not all techniques were used on all compounds. (Tr. 9.16:5-16 (Burnett).) As newly synthesized compounds were tested, the chemists developed hypotheses about how particular structural changes altered the performance of the compounds — for better or for worse. These hypotheses involved what chemists refer to as Structure Activity Relationships ("SAR"). (Tr. 9.13:1-5 (Burnett).)

In order to identify and differentiate between compounds, Schering assigned registration numbers or "Schering Numbers" beginning with the prefix "SCH." The assignment of an SCH number to a compound signified that the compound had been synthesized by a particular process and that certain physical properties of that compound had been identified and reported. Based on the evidence at trial, an SCH number could not be assigned until the compound had actually been synthesized (Tr. 1.198:8-16 (Clader).) However, Schering required no minimum amount of synthesized compound, or a minimum threshold purity level of that compound before an SCH number was assigned to that compound. (Tr. 3.182:2-3 (Rosenblum).) Compounds were not always registered the first time they were made. Compound numbers were normally assigned sequentially based upon the submission date, so a higher SCH number generally indicates a later submission date. (DTX 1331, at 2, DTX 1108).

In the early 1990s, Dr. Duane Burnett designed, synthesized, and tested compounds where the core was structurally constrained to be an azetidinone (beta lactam) ring. (Tr. 9.12:23-9.13:11 (Burnett).) Dr. Burnett also eventually synthesized trans-1, 4-bis-(4-methoxyphenyl1)-3-(3-phenylpropyl)-2-azetidinone and its 3R,4S optically pure isomer, which were assigned Schering Registration Nos. SCH47949 and SCH48461, respectively. SCH47949 was a racemic mixture that included, as one of its constituents, SCH48461.

SCH48461 was the first CAI to go through toxicology studies. The hamster data showed that SCH48461 significantly lowered cholesterol levels, although it performed poorly in the *in vitro* ACAT assay. SCH48461 eventually entered Phase I (safety) and then Phase II (efficacy) human clinical trials. (Tr. 9.35:21-9.36-12 (Burnett).) While SCH48461 had some success in lowering cholesterol, its success was less than anticipated. SCH48461 also yielded adverse side effects in both livers and kidneys of mice. As such, Schering continued to look for a better "back up" compound while investigating the then-unknown mechanisms of action. (Tr. 1.67:3-21 (Afonso).)

Simultaneous with the biology group's testing of SCH48461, the metabolism group was investigating potential metabolites of SCH47949 and SCH48461. These metabolites were of particular interest because Schering scientists believed they might show better activity *in vivo* than the SCH compounds themselves.

The testimony also reflects that, in 1992, Dr. Margaret van Heek joined Schering as a senior scientist in the cardiovascular department. Dr. van Heek was hired to work on the CAI project and was specifically tasked with designing experiments that could elucidate SCH48461's mechanism of action. (Tr. 1.67:21 (Afonso).) One of those experiments was

referred to as the rat bile duct study. As part of that experiment rat bile was collected after SCH48461 had been administered to the rats. Dr. van Heek later readministered that rat bile back into the rats and found that it was more efficacious than SCH48461. Mr. Kevin Alton helped to separate the rat bile into its components or constituent metabolites referred to as "fractions."

Dr. van Heek readministered the separate fractions into the rats and found that one, known as "Fraction 6," was more efficacious compared to the other fractions, including the readministered composite rat bile, and the initial SCH48461. Fraction 6 was the glucuronate of SCH53695, a compound that Schering's chemists had previously made. As the glucuronate of this compound, Fraction 6 was in fact a metabolized, sugar version of the same compound structure as SCH53695. The glucuronate or sugar attaches at the C4 hydroxy (-OH) position of SCH53695. These findings directed the chemists to focus particularly on the C4 area of the molecule.

Based on this work, the chemistry team attempted to synthesize these metabolites. Dr. Yumibe's July 11, 1991 report provided the first structural depictions, absent stereochemistry, of compounds that were later resolved and designated as 4A though 4F. Even without the stereochemistry, Dr. Atwood testified that one skilled in the art could have envisioned all of the stereoisomers, including compounds 4E and F based on a visual inspection of Yumibe's structures. (Tr. 5.99:21.5-101:10 (Atwood).) Accordingly, Mylan asserted at trial that neither Dr. Rosenblum, nor any other member of the chemistry group was the first to conceive of the

structures of compounds 4A through 4F.[2]

As testified at trial, as part of the chemistry group's overall effort to synthesize metabolites of SCH48461, on March 29, 1993, Dr. Rosenblum synthesized a small amount of a mixture of isomers later identified in the '721 and '461 patents as compounds 4A, 4B, 4C, and 4D using a methodology that included a "Grignard" reaction. Dr. Rosenblum then registered this mixture that received the designation SCH55066.

The documentary evidence shows that, in a June 1993 Semi-Annual Progress Report, Dr. Rosenblum reported that "[s]ynthesis of 3' hydroxylated congeners SCH 55066 . . . and chromatographic comparison to *in vivo* derived samples confirms benzylic hydroxylation as a major metabolic pathway." (DTX 73 at -747.) Dr. Rosenblum assigned tentative stereochemistries to 4A and 4B in May 1993, namely 3R and 4S, and 3-prime S for 4B. Compounds 4A and 4B were assigned registration numbers SCH56187 and SCH56191, respectively.

The credible evidence indicates that Dr. Rosenblum, after synthesizing compounds 4A through 4D, turned his focus to trying to synthesize 4E and 4F in or about the Fall of 1993. Documents introduced at trial showed that he detailed and updated these efforts in various internal reports often describing his efforts to make compounds 4E and F as "synthesis in progress." (See e.g., DTX 488; DTX 315.) A memorandum describing a meeting between Drs. Rosenblum, Afonso, Ganguly and Dr. Rosenblum's assistant, Tram Huynh reflects that the synthesis of 4E and 4F, labeled Metabolite #6, remained a goal as of October 18, 1993.

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[2] Dr. Rosenblum had a copy of Yumibe's 1991 report as demonstrated by the notation "SR Copy" on the first page of DTX 1055.

(DTX 485.) Similarly, a memorandum reflecting a consulting session between Dr. Rosenblum and Dr. Derek Barton reflects that as of November 9, 1993, synthesis of 4E and 4F was a "current high priority" for Dr. Rosenblum. (DTX 265 at -204.)

On November 17, 18, and 22, 1993, Dr. Rosenblum recorded the fifth and final step in his attempt to make 4E and F on page 60 of his lab notebook number 31818. Thereafter, Dr. Rosenblum made three separate attempts to synthesize Compounds 4E and 4F using the reaction from the fourth step.

This Court finds that although he synthesized 4A through 4D, Dr. Rosenblum was unable to synthesize 4E and 4F. Dr. Greene, Schering's Director of Cardiovascular, then asked Dr. Afonso to synthesize compounds 4E and 4F. On December 9-10, 1993, Dr. Afonso successfully synthesized compounds 4E and 4F using a biphasic sovolysis process. Compounds 4E and 4F were given Schering registrations number SCH57212 and SCH57214, respectively. The racemic mixture of compounds 4E and F was designated SCH57210. Claims 1, 2, and 7 of the '115 and '721 patents covered compounds 4E and F.

At trial it was also established that, after Dr. Afonso's first synthesis, he and Dr. Rosenblum made more of these compounds using this biphasic solvolysis process. Dr. Rosenblum then submitted these compounds for testing. 4F had the highest activity of any of the then-metabolites of SCH48461.

C. Compounds 6C and 6D

Compounds 6C and 6D are the two additional compounds at issue in this case. It appears to this Court, that the only difference between Compounds 6C and 6D and Compounds 4A and 4B is that 6C and D have an O-acetyl group on the C-4 phenyl ring

whereas Compounds 4A and 4B have a methoxy group in this position. Although, Mylan contends that Dr. Afonso first conceived and synthesized these compounds on December 10, 1993, the Court finds that the evidence does not establish that he first had the idea for the structure of these compounds. Rather this Court finds, although Dr. Afonso was the first to make Compounds 6C and 6D, Dr. Rosenblum gave him the starting materials he needed, with an O-acetyl on the C-4 phenyl. Thus, it is clear, that the starting O-acetyl was present on the C-4 phenyl because Dr. Rosenblum was aware of the final targeted structure of Compounds 6C and 6D, as corroborated by his November 1993 project update. (DTX 265.)

D. Compound 6A (Ezetimibe)

The evidence presented at trial indicates that after 4F was synthesized, Dr. Rosenblum focused his efforts on modifying 4F to block non-productive metabolism. Dr. Rosenblum ultimately did so by substituting a fluorine atom for each methoxy group located at the N1 and C3 phenyl groups of 4F in order to synthesize compound 6A. Accordingly, Compound 4f and ezetimibe have the identical stereochemistry at every stereogenic center.

The Court finds credible and accepts the testimony that Dr. Rosenblum had the idea for the structure of ezetimibe. (Tr. 4:62:23–4.63:3 (Afonso).) Similarly, there is no dispute that Dr. Rosenblum, with the help of his assistant, Tram Huynh made ezetimibe for the first time. Further, the Court finds reasonable, as Schering contended, that Compound 4F was not critical to the discovery of ezetimibe. The credible evidence indicates that by November 9, 1993, Dr. Rosenblum had conceived of the structure of ezetimibe, including its stereochemistry because he was aware of the preferential stereochemistry of Compound 4B as compared to Compound 4A (DTX 265).

After being away from his lab for an extended period of time between mid-December and early February, Dr. Rosenblum returned on February 9, 1994 and immediately began work to complete the multistep synthesis of ezetimibe, which he finished on March 10, 1994. Hamster data for Compound 4F was first recorded on February 16, 1994 and available to Dr. Rosenblum "within a week". (Tr. 3.103:1-3.104:23 (Rosenblum).) Schering claims this is too closely temporally related to the ultimate synthesis of ezetimibe to have played a role in its conception. The Court finds credible that "all of this occurred before Dr. Afonso's mid-December synthesis of Compounds 4E and 4F showing that it played no role in the discovery of the benefits of an OH group on the C-4 phenyl." Pl. Brief at 8, DE # 422 (Jan. 25, 2012).

E. Dr. Afonso's Adverse Inventorship Claims

Dr. Afonso worked at Schering until 1999 when he retired. After Dr. Afonso's retirement in 1999, Schering launched Zetia in the United States in 2002 and Vytorin in 2004. Both contain ezetimibe. In connection with these U.S. launches the named inventors on the '461 patent began to receive awards including the Heroes of Chemistry Award from the American Chemical Society, the Thomas Alva Edison Patent Award from the R & D Council for New Jersey, the National Inventor of the Year Award from the Intellectual Property Owners Education Foundation, and the Prix Galien. (Tr. 9.98:22-9.101:21 (Burnett).)

At trial it was established that, in an e-mail dated November 2002, Dr. Afonso expressed his concern to Dr. Rosenblum concerning the portrayal of the discovery of ezetimibe as it was described in an article published in the Star-Ledger. (DTX 715.) Thereafter, on or about July 6, 2005, Dr. Afonso requested copies of the '115 and '365 patents from Dr. Rosenblum. (DTX 740.) Then on July 15, 2005, Dr. Afonso prepared and sent to

Schering's then-Chief Patent Counsel, James Nelson, a letter requesting that Dr. Afonso's name be added as a co-inventor on the '115 and '365 patents. In the letter, Dr. Afonso indicated that he was originally included on the list of potential inventors for the application leading to the '115 patent, but he instructed Dr. Rosenblum to remove his name. Specifically, Dr. Afonso testified that he asked Dr. Rosenblum to remove his name from the list to ensure that Dr. Rosenblum received credit for the work, despite the fact that Dr. Afonso thought he himself was an inventor and even though other inventors were named. (Tr. 4.14:4-13 (Afonso).) Dr. Afonso claimed this removal was a benevolent gesture: he wanted to promote his protege's career. It was Dr. Afonso's testimony that Dr. Rosenblum's career at Schering had stalled because Dr. Rosenblum had been turned down for a promotion that Dr. Afonso had recommended him for. Dr. Afonso alleges that had he been named as a co-inventor those contributions would have deflected Dr. Rosenblum's recognition. After sending the aforesaid letter to Nelson, Dr. Afonso learned that the '115 patent was reissued as the '721 patent.

According to the evidence, on August 18, 2005, Dr. Afonso met with Auth to discuss his inventorship claim. During the meeting, Auth informed Dr. Afonso that she did not consider him to be an inventor. The next day, Dr. Afonso sent Schering an e-mail dated August 19, 2005. The e-mail was intended for Auth and provided additional information that Dr. Afonso believed supported his inventorship claim. Specifically, Dr. Afonso explained to Auth that he had first synthesized compounds 4E and F, and that the hamster testing of Compound 4F was critical to the discovery of ezetimibe. (Tr. 4.77:9-20 (Afonso); DTX 1005.)

By letter dated November 15, 2005, Auth informed Dr. Afonso that Schering had declined his request to add his name to the patent. Dr. Afonso then sent another letter to

Nelson quarreling with Auth's position. In the letter, Dr. Afonso noted that Dr. Rosenblum had spent months trying to make 4E and 4F but these compounds were not successfully synthesized until Dr. Afonso himself did so in early December 1993.

In a series of e-mails between Dr. Rosenblum and Dr. Afonso on November 30 and December 1, 2005, Dr. Afonso expressed his displeasure with Schering's ultimate inventorship determination. Dr. Afonso believed that Dr. Rosenblum provided "enough negative corroboration," which led to Schering's decision not to add him to the patent.

The Court notes that, during his 2008 deposition, Dr. Afonso vigorously denied having had any deceptive intent when he told Dr. Rosenblum in 1993 that he himself was not inventor. In fact, he testified that he felt "insulted with that question." (Tr. 4.113:3-10 (Afonso).) It also appears that there was no benefit to him having his name removed as an inventor, and had he in fact been listed as an inventor, he nevertheless would have been contractually obligated to assign any of his patent rights to Schering.

F. Prosecution of the '115 Patent

The application for the '115 patent, including the relevant priority applications, were prepared by Schering in-house counsel Anita Magatti. The '115 patent was designated as a continuation-in-part of the prior '440 application as filed in September 1993. According to Ms. Magatti, new patent applications typically resulted from the preparation of an invention disclosure directed to a potential new concept or compound. The invention disclosure included, *inter alia,* a description of the alleged invention, a list of the individuals to be named as inventors, and when it was first reduced to practice. (Tr. 7:13:11-23 (Magatti).)

Ms. Magatti testified that it was her practice to speak with the inventors identified on

the invention disclosure or the designated liaison in order to gather information needed to prepare the draft application, including obtaining information related to the technical examples to be incorporated in the specification. She conceded that in an organization like Schering's, there was an element of prestige associated with being a named inventor on a patent application. (Tr. 7:11:17-21 (Magatti).)

Ms. Magatti could not recall exactly what she did during her preparation of the '115 patent application, but she explained her normal practice. Specifically, she would start by speaking to the inventors identified on the patent disclosure. Then, she would work with the patent liaison on the project team to determine whether other possible inventors should be considered. She testified that she would speak to anyone who had been identified as a possible inventor, to make sure that they understood what inventorship meant and to determine whether they had actually contributed to the conception of the invention. After a draft application had been prepared, it was Magatti's practice to circulate the draft to the inventors. Dr. Burnett added that draft patent applications were sometimes provided to managers and other scientists, even though they were not named inventors. With respect to the application covering ezetimibe, Dr. Burnett testified that he would have expected Dr. Afonso to have received a copy because he was Dr. Rosenblum's supervisor.

G. Prosecution of the '721

The claims of the '721 patent are identical to the claims of the '115 patent, except for the addition of compound, pharmaceutical composition, and method of treatment "bullet claims" that are limited to ezetimibe alone. (Compare DTX 510 ('115 Patent) with DTX '512 ('721 Patent).) Schering did not amend the list of inventors to add Dr. Afonso as an inventor

on the '721 Patent.

For the purposes of this case, the sole disputed issue relating to the '721 patent is whether Dr. Rosenblum or Dr. Afonso committed inequitable conduct by not telling the Examiner, during the reissue proceeding which led to the '721 patent, that Dr. Afonso was an inventor of the claims' subject matter. However, there is no evidence that either doctor was even aware of the reissue at the time, much less that either of them was substantively involved in it. To the contrary, Dr. Afonso testified that when he wrote his July 2005 letter to Nelson, he was not aware that the '115 patent had been reissued as the '721 patent in May 2002.

H. '461 Reissue Proceeding

The application for the '461 reissue patent was prepared and prosecuted by attorneys at the firm of Ropes & Gray, and in particular Messrs. James Haley and Carl Morales. Schering's Legal Director of Patents, Mark Russell, was also directly involved in the reissue process on behalf of Schering. To initiate the resissue proceeding, Schering submitted a "reissue declaration," which was prepared using a Patent Office form. Russell signed the reissue declaration because the '461 patent related to Zetia®, and Zetia® was one of the products that he had supported in the patent department.

According to Schering, Russell's concerns about the potential invalidity of the '721 patent claims were based on earlier litigation with Glenmark Pharmaceuticals, Inc. USA ("Glenmark"). Glenmark argued that Claims 1, 2, 4, and 5 were invalid due to inherent anticipation. Mylan's expert John Goolkasian conceded that this is a proper basis for a reissue. Further, according to Goolkasian, once a proper basis for a reissue is put forward, the patent owner is free to make other narrowing changes in the claims even beyond the identified

error(s).

During the reissue proceeding, the remarks that accompanied the Preliminary Amendment stated that "at least claims 1 of the '721 reissue patent (also claim 1 of the '115 patent) may claim more than the patentee had a right to claims because this claim is potentially inherently anticipated by" the '048 PCT. (DTX 1777.) Schering contends, that in light of Glenmark's contentions —that the '048 PCT reported the *in vivo* administration of compounds, including SCH 48461 — the claims were being amended "to exclude compounds 4A, 4B, 4E and 4F, as well as any other putative metabolites of the Example 9 Compound (and any other of the exemplified compounds) of the '048 PCT publication."

At trial, Mylan's expert Paul Hieble admitted during cross-examination that, as a result of the reissue, millions of other compounds had also been removed from the scope of the claims. Nevertheless, Mylan claims that with the exception of compounds 4A, 4B, 4E and 4F none of the additional compounds removed from the claims were properly considered putative metabolites. Accordingly, Mylan argues that Schering's assertion that the claim amendments deleted compounds that were putative metabolites of the Example 9 compound from the '048 PCT publication is not credible.

Dr. Afonso was not named as an inventor of the '461 patent, but according to Schering Dr. Afonso's claim of inventorship was disclosed during the reissue proceeding. The evidence at trial demonstrates that the Examiner was given a copy of Glenmark's trial brief in the earlier litigation. The Examiner was also apparently given a copy of Mylan's amended answer in the instant litigation. Both documents describe Dr. Afonso's inventorship-related contentions in detail. Mylan however, underscores that the evidence indicates that at no time

did Schering's counsel provide a copy of Dr. Afonso's July 15, 2005 letter to Nelson to the PTO, and further that any references to Dr. Afonso's inventorship claims were buried in the over 10,000 page submission Schering made to the PTO in connection with the '461 reissue proceeding. Accordingly, Mylan contends that the evidence establishes that Schering committed inequitable conduct by breaching their duty to disclose.

I. Brisbois Experiment

At trial Schering called Professor Brisbois as an expert witness. Professor Brisbois testified that he recreated Dr. Rosenblum's method of making Compounds 4E and 4F. He assessed whether he had made these compounds by testing his final reaction product using proton NMR's, infrared spectroscopy, and mass spectroscopy. According to Dr. Brisbois, no compounds other than 4E and 4F could have generated his results. Further, Professor Atwood was unable to identify one compound, other than Compounds 4E and F that could have generated the results that Dr. Brisbois obtained.

At trial, Mylan contested the credibility of Professor Brisbois' testimony and alleged that his experiment was not exactly a faithful reproduction of Dr. Rosenblum's work. Dr. Atwood identified several differences between the protocol that Dr. Rosenblum and Huynh used, and the one that Professor Brisbois performed. For example, at step 2 of the 5-step process, Huynh heated the material to reflux at 80 degrees celcius. Dr. Atwood testified that Huynh must have made an error because toluene would not have refluxed at 80 degrees. Dr. Atwood noted that Huynh must have made an error reading the thermometer, but it was unlikely that she would be mistaken as to whether something was boiling or not. Huynh also indicated that she kept the reaction at reflux overnight, and unlike Huynh, Brisbois kept the

reaction at 80 degrees celcius without taking it to reflux. In another example, at step 2, Huynh crystallized the beta lactam out of the solution, whereas Brisbois rotovaped the product out of solution. Dr. Brisbois contends that even if he deviated from Dr. Rosenblum's process, the alleged changes should have made the reaction less successful, not more so.

After performing the experiment, Brisbois stored the mixture in the freezer for two weeks. On February 11, 2009, Brisbois removed the material and carried out another TLC experiment to confirm that the sample had maintained its structural identity. Brisbois recorded the February 11, 2009 TLC plate in his lab notebook, but destroyed the original TLC plate. Based on the depiction of the TLC plate in the notebook, the Rf value of the relevant sport on Brisbois February 11, 2009 plate was 0.25, whereas on January 29, 2009 it was 0.45. The difference in the Rf value is material because it reflects that the compound has structurally changed during the time it was stored.

II. LEGAL STANDARD

A. Jurisdiction

This Court has subject matter jurisdiction over this action under 28 U.S.C. §§ 1331 and 1338(a). Venue is proper in this judicial district pursuant to 28 U.S.C. §§ 1391(c) and 1400(b), and the Court has personal jurisdiction over the parties. Mylan admits that Schering and MSD International GmbH have standing to bring this action.

B. Inventorship

An issued United States patent "shall be presumed valid." 35 U.S.C. s. 282. Accordingly, the "burden is on the party asserting invalidity to prove it with facts supported by clear and convincing evidence." Linear Tech Corp. v. Int'l Trade Comm'n, 566 F.3d 1049,

1066 (Fed. Cir. 2009) (internal citations omitted). Moreover, any testimony from a person claiming inventorship status "must be corroborated by independent evidence." Cooper v. Goldfarb, 154 F.3d 1321, 1330 (Fed. Cir. 1998). Independent, corroborating evidence is required "to prevent fraud, by providing independent confirmation" of the alleged "inventor's testimony." Kridl v. McCormick, 105 F.3d 1446, 1450 (Fed. Cir. 1997). Further, the corroboration requirement is necessary because years after the issuance of a patent, even "honest witnesses can convince themselves that they conceived the invention of a valuable patent." Price v. Symsek, 988 F.2d 1187, 1195 (Fed. Cir. 1993). The patent statute also provides for the routine correction of inventorship if the wrong inventors are named on a U.S. patent. 35 U.S.C. § 256 ("Whenever through error a person is . . . not named in an issued patent and such error arose without any deceptive intention on his part, the Director may . . . issue a certificate correcting such error.").

"Conception is the touchstone of inventorship," and it is the "formation in the mind of the inventor, of a definite and permanent idea of the complete and operative invention as it is hereafter to be applied in practice." Burroughs Wellcome Co. v. Barr Labs., Inc., 40 F.3d 1223, 1227-38 (Fed. Cir. 1994). A "joint inventor must contribute in some significant manner to the conception of the invention" and "a contribution to conception is a mental act." Fina Oil & Chem. Co. v. Ewen, 123 F.3d 1466, 1473-74 (Fed. Cir. 1997). In the case of a new compound, conception normally "requires 1) the idea of the structure of the chemical compound, and 2) possession of an operative method of making it." Oka v. Youssefyeh, 849 F.2d 581, 583 (Fed. Cir. 1988). Reduction to practice can be probative of these elements, but is not dispositive of the issue of inventorship. Notably, to prevail, Mylan would have to show

not just that Dr. Rosenblum did not have an operative method of making these compounds, but that none of the named inventors possessed this skill.

C. Inequitable Conduct

To prove inequitable conduct, Mylan must demonstrate that Dr. Rosenblum or Dr. Afonso "misrepresented or omitted material information with specific intent to deceive the PTO." Therasense, Inc. v. Becton Dickinson & Co., 649 F.3d 1276, 1287 (Fed. Cir. 2011) (en banc). The materiality required to establish inequitable conduct is but-for materiality. In other words, "the PTO would not have allowed a claim had it been aware of the undisclosed information." Id. at 1291. In making this patentability determination, "the court should apply the preponderance of the evidence standard and give claims their broadest reasonable construction." Id. at 1291-92.

In addition to the materiality prong, Mylan must prove by clear and convincing evidence, that the actors in question acted with the specific intent to deceive the PTO. Id. at 1290. It is not enough to establish that the patent applicant had a generalized intent to deceive or withhold. Rather, under Therasense, a "specific intent" to deceive must be proven by demonstrating by clear and convincing evidence "that the applicant knew of the reference, knew that it was material, and made a deliberate decision to withhold it." Id. at 1290. To meet the clear and convincing evidence standard, the specific intent to deceive must be the single most reasonable inference able to be drawn from the evidence." Id. Under Therasense, where "there are multiple reasonable inferences that may be drawn, intent to deceive cannot be found." Id. at 1290-91. The patentee need not offer any good faith explanation unless the accused infringer first proves "a threshold level of intent to deceive by clear and convincing

evidence." Id. at 1291.

III. DISCUSSION

Mylan maintains that Dr. Afonso was omitted from the '461 patent as a result of a deceptive intention on the part of Dr. Afonso and Dr. Rosenblum. As such, this failure to name Dr. Afonso as an inventor, according to Mylan, makes the '461 patent invalid. Mylan also takes the position that Dr. Afonso and Dr. Rosenblum, and the participants in the reissue proceedings, deliberately deceived the Examiner by not revealing that Dr. Afonso was a co-inventor of the '461 patent and its two predecessor patents, the '721 and '115 patents respectively. The Court will treat each of these issues separately.

A. Inventorship

As previously stated, in the case of a new compound, an inventor is said to have conceived of it if he or she 1) had the idea of the structure of the chemical compound, and 2) possessed an operative method of making it. Oka v. Youssefyeh, 849 F.2d 581, 583 (Fed. Cir. 1988). The actual making of the compounds, or "reducing them to practice" is not required for inventorship. Burroughs Wellcome Co. v. Barr Labs., Inc. 40 F.3d 1223, 1227-28 (Fed. Cir. 1994). Dr. Afonso's and Mylan's claims arise out of Dr. Afonso's ability to make the Compounds 4E, 4F, 6C, and 6D, and whether Dr. Afonso was thus the first to possess an operative method. If he was the first to possess an operative method, he would be a co-inventor as he satisfies the second prong of the inventorship test.

Mylan's contention at trial focused on the fact that Dr. Rosenblum's failed attempts to make Compounds 4E and 4F prior to Dr. Afonso shows that he had no operative method to make them. However, the sequence of events as illustrated by the credible evidence

undermines Mylan's argument and its ability to meet its clear and convincing burden on this issue.

Evidence at trial indicated that by July 1, 1993, Dr. Rosenblum had hamster data that showed that Compound 4B, which has a similar stereochemistry that was later incorporated into ezetimibe performed better than Compound 4A. This is evidence tends to indicate, as Schering argued, that by November 1993 Dr. Rosenblum had conceived of the structure of ezetimibe because he was aware of the preferential stereochemistry of Compound 4B as compared to Compound 4A. He directed his assistant to begin the synthesis of the "fluorinated series" of compounds, which includes ezetimibe. Ms. Huynh made the starting material on November 23, 1993. Dr. Rosenblum was away from the lab between mid-December 1993 and early February 1994. He returned to work on February 9, 1993 and began work to complete the multistep synthesis of ezetimibe, which he finished on March 10, 1994.

The evidence as it pertains to Compound 4F indicates that hamster data for Compound 4F was first recorded on February 16, 1994 and available to Dr. Rosenblum "within a week." Here, although Mylan argues that this data thus played a role in Dr. Rosenblum's idea for the structure of ezetimibe, this is not the single most reasonable inference as the clear and convincing burden requires. While Mylan's argument is plausible, the temporal relationship between the availability of the hamster data and the ultimate synthesis of ezetimibe in fact reasonably indicates that it did not play a role in Dr. Rosenblum's idea for the structure of ezetimibe. This inference is further supported by the aforesaid evidence regarding Compound 4B and Dr. Rosenblum's conception of Compounds 6C and 6D.

Similarly, Mylan contended at trial that Dr. Rosenblum got the idea for the OH on the

C-4 phenyl of ezetimibe from the hamster data for Compounds 4E and 4F, which also have an OH in that position. However, again the chronology of events as disclosed at trial does not raise Mylan's contentions to the necessary clear and convincing burden of proof. Dr. Rosenblum testified that he was aware of the specific benefits of the C-4 OH during 1993 as demonstrated by his December 1, 1993 semi-annual report, before Dr. Afonso's mid-December 1993 synthesis of Compounds 4E and F.

The determination is the same when one applies the inventorship analysis to Afono's biphasic solvolysis process. Even if Dr. Afonso's process was the first operative way to make Compounds 4E and 4F, his process was not novel as it was described in a 1986 paper published in the *Journal of Medicinal Chemistry*. (PX 483.) As such, Dr. Afonso did not contribute to the invention of Compounds 4E and 4F because he did not first conceive the operative method he used to make them. Rather his synthesis of Compounds 4E and F only constitutes the first successful execution of this process for the purpose of making 4E and F. As the Federal Circuit explained in Falana, "simply teaching skills or general methods that somehow facilitate a later invention, without more, does not render one a co-inventor." 2012 U.S. App. LEXIS 1245 (Fed. Cir. Jan. 23, 2012).

The Court finds that, Mylan has further failed to provide corroborating evidence that is clear and convincing. Despite some circumstantial evidence reflecting a potential contribution of varying degrees by Dr. Afonso to the inventions of Compounds 4E and 4F and ultimately ezetimibe, no fact witness, other than Dr. Afonso, testified that Dr. Afonso made any contribution to the stereochemistry that Dr. Rosenblum selected for ezetimibe, which is actually claimed in the patent-in-suit. Nor is there any contemporaneous physical or

documentary evidence showing that Dr. Afonso's work contributed to Dr. Rosenblum's idea for the stereochemistry of ezetimibe. Rather, Mylan attempts to meet its burden of proof by relying on the close temporal relationship between the availability of the hamster data and the ulitimate synthesis of ezetimibe. This fails to establish that the single most reasonable inference from this information is that Dr. Rosenblum relied on this information. Had there been some credible evidence introduced by way of a report, notebook, or witness testimony, that affirmatively established a relationship between the aforesaid available data and the creation of ezetimibe, this Court's calculus may have been different. However, in light of the credible evidence which was in fact presented, Mylan has failed to meet their clear and convincing burden.

The Court also notes that the patent-in-suit does not claim Compounds 4E and 4F. Mylan argues that Dr. Afonso made an inventive contribution to ezetimibe, which is claimed in the '461 patent, because he was the first to synthesize compounds 4E and 4F. According to Mylan, the successful synthesis of 4F and its subsequent performance in the hamster tests gave Dr. Rosenblum the idea for the stereochemistry of ezetimibe. Thus, Mylan's purported assignment of inventorship would require this Court to assign credit for work by Dr. Afonso that is one step removed from the patent in question. In other words, Mylan wants to invalidate the patent-in-suit based on compounds and methods that were claimed in the predecessor patents.

Even if Dr. Afonso was an inventor of Compounds 4E and 4F and should have been named in the predecessor patents, this argument would only be grounds to invalidate the patent based on inequitable conduct under the Doctrine of Infectious Unenforceability. It does

not change the inventors of the patent-in-suit. There can be no dispute as to who ultimately conceived and possessed an operative method of making ezetimibe. At best, Dr. Afonso made a contribution that either inspired or informed the ultimate invention of ezetimibe, which is not sufficient to render him an inventor of the compounds claimed in the patent-in-suit. That ezetimibe may never have been invented without Dr. Afonso's first successful synthesis of compounds 4E and 4F is 1) speculative, and insufficient to meet the clear and convincing burden, and more importantly, 2) does not change the analysis with respect to inventorship of ezetimibe. Mylan's adverse inventorship claims with respect to compounds 4E and 4F may or may not indicate inequitable conduct, but they do no properly challenge who first conceived and developed an operative method of creating ezetimibe.

As discussed, conception is a "mental act." Fina Oil, 123 F.3d at 1473. Conception of a chemical compound "requires identification of the specific chemical structure of the compound," Vanderbilt Univ. v. Icos Corp., 601 F.3d 1297, 1301 (Fed. Cir. 2010), and does not occur "unless one has a mental picture of the structure of the chemical" or "whatever characteristics sufficiently distinguish it." Bd. of Educ. v. Am. Bioscience, 333 F.3d 1330, 1340 (Fed. Cir. 2003). Accordingly, even if Compound 4F informed Dr. Rosenblum's choice of ezetimibe's structural features, which is contested, that would be insufficient to elevate Dr. Afonso to inventorship status with respect to ezetimibe.

B. Inequitable Conduct

1. The Predecessor Patents, '115 and '721

Mylan contends that Dr. Rosenblum and Dr. Afonso committed inequitable conduct with respect to the '115 and '721 predecessor patents. To meet their burden, Mylan must

prove that Dr. Rosenblum or Dr. Afonso "misrepresented or omitted material information with the specific intent to deceive the PTO." Therasense, Inc. v. Becton, Dickinson & Co., 649 F.3d 1276 (Fed. Cir. 2011) (en banc). It is not enough to establish "that the patent applicant had a generalized intent to deceive or withhold." Preview Interactive, Inc. v. Starsight Telecast, Inc., No. 93-cv-934, 1999 U.S. Dist. LEXIS 1956 at *21 (N.D. Okla. Feb. 19, 1999). Instead, under Therasense, a specific intent must be proven. 649 F.3d at 1290. As previously stated, the required materiality, is "but-for," meaning that the PTO would not have allowed a claim had it been aware of the undisclosed" information. Id. at 1291. This determination is made based upon a preponderance of the evidence. Id. at 1291-92. Further, as the '115 and '721 patents are not asserted in this action, Mylan must show that the doctrine of infectious unenforceability applies.

Mylan contends that Dr. Afonso contributed to the conception of four compounds that were named in the '115 and '721 predecessor patents, but not in the '461 patent: Compounds 4E, 4F, 6C, and 6D. Therefore, the question for this Court is whether, based on a preponderance of the evidence, Dr. Afonso made an inventive contribution to the invention of these compounds.

Based on the credible evidence presented at trial, the Court finds that Mylan has failed to establish that Dr. Afonso was an inventor of the four compounds at issue that were claimed in the predecessor patents. With respect to Compounds 6C and 6D, and as the Court has previously stated, although Dr. Afonso was the first to actually synthesize Compounds 6C and 6D, Dr. Rosenblum gave him the starting materials he needed, with an O-acetyl on the C-4 phenyl. It is clear, that the starting O-acetyl was present on the C-4 phenyl because Dr.

Rosenblum was aware of the final targeted structure of Compounds 6C and 6D, as corroborated by his November 1993 project update. (DTX 265.)

Further, with respect to Compounds 4E and 4F, Mylan failed to prove that Dr. Afonso made a contribution to the invention of these compounds beyond their first synthesis. Rather, the evidence at trial suggests that these compounds were first conceived by Drs. Burnett and Clader as demonstrated by the '440 application. In fact, according to Professor Roush, if a chemist had been able to make Compound 8F, as Dr. Burnett had done, that chemist would have also been able to make Compounds 4E and F after routine experimentation. Indeed, it is clear that as of December 1993, the named inventors could have used multiple methods named in this application to synthesize 4E and F with routine experimentation. Therefore, Dr. Afonso did not contribute the operative method of making Compounds 4E and 4F to their invention.

Whether Dr. Afonso was the first or second person to actually synthesize Compounds 4E and 4F makes no difference, because reducing the compound to practice does not make a person an inventor. Rather, one needs to demonstrate conception and an operative method of creation; neither of which Mylan has proven that Dr. Afonso contributed. Even if Dr. Afonso's method represented the best mode for making these Compounds at that time, this fact alone does not make him an inventor because 1.) this Court has found that his process was not novel; and 2.) "one of ordinary skill in the art who simply reduced the inventor's idea to practice is not necessarily a joint inventor, even if the specification discloses that embodiment to satisfy the best mode requirement." Ethicon, 135 F.3d at 1460.

Accordingly, because the Court has determined that Dr. Afonso was not an inventor of

Compounds 4E, 4F, 6C and 6D, the most reasonable inference is that, during prosecution of the '115 patent, neither Dr. Afonso, nor Dr. Rosenblum, believed Dr. Afonso was an inventor. As such, they could not have an the requisite intent to deceive the PTO as required to establish inequitable conduct. Furthermore, this Court has already determined the inventors did not have the requisite knowledge of the '721 reissue to engage in deception of the PTO. Therefore, Dr. Rosenblum and Dr. Afonso did not engage in inequitable conduct with respect to this predecessor patents either.

2. The Patent-in-Suit, '461

Because this Court has determined that Dr. Afonso was properly not named as an inventor on the predecessor patents, the Doctrine of Infectious Unenforceability is not at issue. The question remaining for the Court is whether the '461 reissue was properly invoked. In making this assertion, Mylan bears a burden of proof by clear and convincing evidence.

Under the reissue statute, a reissue proceeding can be initiated "wherever any patent is, through error without deceptive intention, deemed wholly or partially inoperative or invalid, by reason of defective specification or drawing . . ." Schering sought reissue of the '721 because, according to its reissue declaration signed by Mark Rusell "at least claim 1 of [the '721] is potentially anticipated by [the '048 PCT] . . ." Russell's concerns were grounded in issues arising during the Glenmark litigation. There is no dispute that this stated basis is a proper basis for a reissue. (Tr. 8.75:19-25 (Goolkasian).)

Once a proper basis for reissue is asserted, other narrowing changes to the patent's claims can be made without explanation. As stated by Mylan's expert, John Goolkasian, PTO rules do not require that the reasons for any other changes be communicated to the Examiner.

Because the reissue proceeding constitutes a proper invocation of the reissue statute, and further, because this Court has found that Dr. Afonso was not an inventor of the Compounds claimed in the predecessor patents, the most reasonable inference is that no inequitable conduct was committed.

Accordingly, this Court finds also that Mylan failed to prove that Russell, Haley and Morales committed inequitable conduct. In order to demonstrate that these attorneys committed inequitable conduct, Mylan had to prove an intent to deceive on their parts. Specifically, Mylan must have demonstrated that the attorneys believed the stated justification for the reissue proceeding was false and therefore intended to deceive the Examiner. Based on the evidence at trial, the Court does not find this allegation credible. Rather, the most reasonable inference is that the attorneys identified the metabolite related error because they believed it to be legitimate. It is not because, as Mylan would have this Court believe, because Schering was trying to remove traces of Dr. Afonso's work. This allegation is exceptionally incredible in light of this Court's determination that Dr. Afonso was not an inventor of the compounds claimed in the predecessor patents and removed during the '461 reissue. Furthermore, Mylan failed to satisfy the but-for materiality prong because, without a deception, there can be no alternate determination regarding patentability that the PTO would have made. Indeed, this Court finds that Schering did not withhold any material information regarding Dr. Afonso's adverse inventorship claim because 1.) Schering properly determined that Dr. Afonso was not actually an inventor; and 2.) Dr. Afonso's adverse inventorship claims were referenced in the Glenmark litigation documents provided to the PTO by Schering during the reissue.

Accordingly, this case is distinguishable from the Federal Circuit's recent decision in Aventis Pharma. S.A. v. Hospira, Inc., No. 11-1018 (Fed. Cir. Apr. 9, 2012) wherein the Court held that the inventor intentionally withheld references that were material to patentability from the PTO.[3] In the instant case, the Court finds that based on the evidence, Dr. Rosenblum and Dr. Afonso did not intend to deceive the PTO during the '115 patent application. Rather, the Court finds that, both Drs. Rosenblum and Afonso made a reasonable determination that Dr. Afonso was not an inventor. As to the '721 patent, it is not even clear that Drs. Afonso and Rosenblum even knew of this reissue at the time it took place, and therefore could not have intended to deceive the PTO. Furthermore, during the '461 reissue, the evidence indicates that the attorneys believed the metabolite-related error was a sufficient basis to invoke a reissue as had been demonstrated to them during the Glenmark litigation. Lastly, Mylan failed to prove both that Plaintiff actually even deceived the PTO and thus did not establish but-for materiality, because Dr. Afonso's adverse inventorship claim is referenced in the Glenmark litigation documents that were provided to the PTO during this proceeding.

[3] This case is significant because it demonstrates that inequitable conduct can still be proven even after Therasense; however, it does not change the Court's analysis here.

IV. CONCLUSION

For the foregoing reasons, the '461 patent is hereby declared valid and enforceable. No inequitable conduct determination shall issue. An appropriate order accompanies this opinion.

DATED: April 27, 2012

JOSE L. LINARES
U.S. DISTRICT JUDGE